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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/844,864	04/27/2001	Martin M. Matzuk	P01925US2 (09807797)	1363

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EXAMINER	
WILDER, CYNTHIA B	

ART UNIT	PAPER NUMBER
1637	

DATE MAILED: 05/14/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/844,864	MATZUK ET AL.	
	Examiner	Art Unit	
	Cynthia B. Wilder, Ph.D.	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 February 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *23,24 and 26-28* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *23, 24, 26-28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on February 25, 2004 has been entered.

Status of Claims:

Claims 23, 24 and 26-28 are pending.

Claims 1-22 and 25 have been canceled.

Claim Rejections - 35 USC § 101

2. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The pending claims have been reviewed in light of the Utility Examination Guidelines and Guidelines for Examination of Patent Applications under 35 U.S.C. 112, first paragraph "Written Description" requirements, Federal Register, Vol. 66, No. 4, pages 1092-1111, Friday, January 5, 2001.

A well established utility is defined as a specific, substantial and credible utility which is well known, immediately apparent or implied by the specification's disclosure of the properties of a material, alone or take with the knowledge of one skilled in the art. The instant invention does not have a well established utility because the art does not teach any utility for the instantly

claimed polynucleotides that is specific, substantial and credible. In addition, further characterization of the claimed subject matter would be required to identify or reasonable confirm a "real world" use.

Claims 23, 24, 26-28 are rejected under 35 U.S.C. 101 because the claimed inventions lack patentable utility due to its not being supported by a specific, substantial, and/or credible utility, or, in the alternative, a well-established utility. The claimed inventions are drawn to an isolated polynucleotide having the polynucleotide sequence set forth in Figure 25 (SEQ ID NO: 16) (claim 23), an isolated polynucleotide that specifically hybridizes with the polynucleotide of claim 23 under hybridization conditions of about 0.3 M NaCl at temperatures of about 50 degrees Celsius to about 55 degrees Celsius, wherein the encoded protein modulates fertility (claim 24) or modulates ovarian development or ovarian function (claim 27) and an isolated nucleic acid that is fully complementary to the polynucleotide sequence of claims 23, 24 or claim 27).

The specification teaches at Figure 25 and in the "Brief Description of the Drawing" at page 13, that SEQ ID NO: 16, which is depicted as Figure 25, is the nucleotide sequence of human O1-236 gene or human NPM2 gene. The specification discloses at page 6 that the O1-236 gene is one of three genes that is ovary-specific and/or oocyte-specific. The specification discloses that these genes and their protein products appear to relate to various cell proliferative or degenerative disorders, especially those involving ovarian tumors, such as germ cell tumors and granulosa cell tumors, or infertility, such as premature ovarian failure. The specification teaches at page 13 that the O1-236 gene expression is highly tissue-specific, being expressed in cells primarily in ovarian tissue. The specification further states that based on the know activity

of many other ovary specific proteins, it can be expected that O1-236, as well as fragments and derivatives thereof, will possess biological activities that will make them useful as diagnostic and therapeutic reagents. Nowhere else in the specification is there a teaching of the function of the human O1-236 gene or the encoded protein of said gene. The examples beginning at page 28 through page 46 of the specification discloses the *mouse O1-236 (npm2)* gene (see Figure 5 and SEQ ID NO: 5) and uses of the mouse O1-236 gene in expression analysis with no known function, in cloning procedures, in structural analysis, in chromosomal mapping studies, in subtraction hybridization methods, in knockout mouse protocols, in fertility studies and ovarian-specific expression and *not the human O10236 (npm2) gene.* The specification however fails to provide a specific asserted utility for the polynucleotides as claimed, the human O1-236 polynucleotide and encoded protein. No direct connection is made between the claimed polynucleotide (human O1-326 (NPM2)) and utility as a modulator of fertility or modulator of ovarian development or ovarian function or association with ovarian tumors. In fact, there is no disclosure anywhere in the specification providing support for a use of the human 01-236 polynucleotide, fragment thereof, or the encoded protein. Merely stating that expression of the O1-236 gene is highly tissue-specific cannot be translated to mean that that sequence is necessarily a marker of ovarian tumors or modulator of fertility or modulator of ovarian development or ovarian function in that tissue. Furthermore, there is no apparent *indicia* of specificity to any disease or ovarian developmental stage. Since the specification sets forth no specific function of the polynucleotide or gene sequence for the claimed SEQ ID NO: 16, or provide any guidance for use of the claimed sequence of SEQ ID NO: 16 or fragments thereof, the claimed encoded protein or its use has no ascribed function as well. Therefore, identifying

and/or studying the claimed polynucleotides of the instant invention or fragments thereof or the encoded protein does not define "a real world" context of use because further experimentation would be required to establish a "real world" utility for such sequence that is specific, substantial or credible.

As noted by *Brenner V. Manson*, 383 U.S. 519, 535-536 (1996), "Congress intended that "no patents be granted on a chemical compound whose sole "utility" consists of its potential role as an object of use-testing...a patent is not a hunting license. It is not a reward for the search, but compensation for the successful conclusion". Neither the specification as filed nor any art of record discloses or suggests any property or activity for the claimed polynucleotide sequences such that another non-asserted utility would be well established for the compounds. Therefore, fore all of the foregoing, the claimed inventions are not supported by either a specific and substantial asserted utility or a well-established utility. Note, because the claimed invention is not supported by a specific and substantial asserted utility for the reasons set forth above, credibility has not been assessed.

Claim Rejections - 35 USC § 112, first paragraph

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 23, 24, 26-28 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention. Moreso, one skilled in the art would not know how to use the

claimed invention to modulate fertility or modulate ovarian development and/or ovarian function.

Claim Rejections - 35 USC § 112, First paragraph: Lack of Adequate Written Description

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 24, 26-28 rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claimed inventions are drawn to an isolated polynucleotide that specifically hybridizes with the polynucleotide of claim 23 under hybridization conditions of about 0.3 M NaCl at temperatures of about 50 degrees Celsius to about 55 degrees Celsius, wherein the encoded protein modulates fertility (claim 24) or that modulates ovarian development or ovarian function (claim 27) and an isolated polynucleotide that is fully complementary to claim 23 or claim 24 or claim 27 (claims 26 and 28). The specification does not disclose or describe a sequence wherein the encoded protein of SEQ ID NO: 16 modulates fertility or wherein the encoded protein modulates ovarian development or ovarian function. The specification does not disclose or define what is meant by "modulates" in relations to fertility. Nor is thee a limiting definition in the specification to define what is meant by modulation in relations to ovarian development or ovarian function. For example, it cannot be determine if modulates means that

the hybridizable nucleic acid molecules increase or enhance or decrease or disrupt ovarian development and/or function or fertility functions. There is no mention anywhere in the specification wherein the function of the claimed polynucleotide is disclosed or defined or a correlation between fertility, ovarian function or ovarian development and the polynucleotides of the instant invention. The examples beginning at page 28, especially examples 10-14, examine fertility and sub-fertility in the *mouse npm2* gene which is depicted as SEQ ID NO: 5 and not the human npm2 gene as recited in SEQ ID NO: 16 of the instant claims. None of the examples examined ovarian development and/or function as it relates to the claimed polynucleotide sequences. The examples merely demonstrated an over-expression of a mouse Npm2 gene in ovarian tissue, which does not equate to a function of modulating ovarian development and ovarian function. The claims as written encompass a large genus of hybridizable nucleic acid molecules or complement sequences not adequately described or disclosed. Each of the claimed inventions is a genus for which a representative number of species for each genus must be disclosed to meet the written description requirement of 112, first paragraph. As set forth in the Court in *Vas Cath Inc. V. Mahurkur*, 19 USPQ2d 1111, the written description must convey to one of skill in the art "with reasonable clarity" that as of the filing date, applicant was in possession of the claimed invention. Absent a written description disclosing a representative number of species of the isolated polynucleotides of claims 24, 26-28, the specification fails to show that applicant was, in fact, "in possession of the claimed invention" at the time of the application for patent was filed.

Applicants' Traversal

6. Applicant traverses the rejection on the following ground(s): Applicant states that well-known case law supports Applicant's position. Applicant states that Applicants asset that the claims are described and enabled such that one of skill in the art would be able to determined which hybridizable nucleic acid sequences are claimed. Applicant states that pages 35-36 discuss utilizing an "O1-236 fragment" to measure Npm2 RNA levels. Applicants state that thus fragment was used under the conditions as claimed to hybridize to NPM2 molecules. Applicant states that the Examiner may not have established the link that the term "01-236" is interchangeable with "NPM2". Applicant states that for example the claim 24 depends from the claim 23 which the polynucleotide of sequence of SEQ ID NO: 16 or Figure 25. Applicants state that Fig. 25 clearly indicates that the sequence id the human NPM2 sequence. Applicant s states in the original claims as filed one of skill in the art would infer that O1-236 is NPM2 because the claims state that "O1-236 (NPMP2)". Applicants states that still further on page 13, lines 3-4, the specification states that "nucleotide and amino acid sequence O1-236 (SEQ Id NO: 16). Applicant states that thus, one of skill in the art would infer that O1-236 is NPM2

Applicants further contend that the Examiner indicates that the specification does not disclose or describe an isolated sequence that hybridizes to the polynucleotide sequence of Claim 23. Applicants state that the specification clearly indicates that an "O1-236 fragment" can be used to identify sequences that hybridizes to O1-236 and have the indicated function. Applicants state that the O1-236 fragment was used under specific hybridization conditions in Northern blot analysis and in situ hybridization to determine mRNA expression of Npm2. Applicants states that the specification teaches using the O1-236 fragment to screen cDNA

libraries to identify NPM2 sequences. Applicants assert that the specification teaches polynucleotide sequences that hybridize to the polynucleotide sequence of claim 23.

Applicant states that the Examiner indicates that the specification does not disclose or describe a sequence wherein the encoded protein modulates fertility and/or ovarian development or function. Applicant states that the specification on page 41, examples 12 and 13, Applicant provides evidence that NPM2 modulates fertility and/or ovarian development or function. Applicant states that specifically, the example and tables 5 shows that deficiency of NPM2 resulted in subfertility and infertility in females, but not males. Applicants assert that one of skill in the art would be fully aware that the terms "O1-236" and "NPM2" are interchangeable and that the specification clearly demonstrates that NPM2 modulates fertility and/or ovarian development or function.

Examiner's Response

7. Applicant's arguments filed on February 25, 2004 have been thoroughly reviewed and considered, but they are not found persuasive for the following reasons: The examiner acknowledges Applicants' arguments that the term "O1-236" and "NPM2" are interchangeable. However, it is noted that the specification teaches **two different** "O1-236" genes or "NPM2" gene, one isolated from the mouse (SEQ ID NO: 5) and one isolated from human (SEQ ID NO: 16). While the specification teaches in the examples, experiments associated with the mouse O1-236 gene or mouse NPM2 gene, no disclosure was found correlating or examining the human Npm2 or O1-236 gene with any ascribed function. The examples, as noted by Applicant, especially example 12, examined infertility and sub-fertility in the mouse models based on a deficiency of mouse Npm2 expression and *not* human Npm2 expression. The example showed

wherein a deficiency of the Npm2 expression (mouse) resulted in a decrease or lack of fertility. The specification however does not teach an isolated nucleic acid molecule that (increase or decrease) modulates fertility in human or human cells based on the presence or lack of the human Npm2 gene. Likewise, there is no disclosure anywhere in the specification demonstrating modulation of ovarian development or ovarian function based on the presence or absence of the human Npm2 gene. To reiterate, the specification only demonstrates over-expression in ovarian tissue which clearly cannot be translated as a function in that tissue. Thus contrary to Applicant's arguments, the specification does not support the claims 24, 26-28. Accordingly, the specification fails to show that Applicant was, in fact, "in possession of the claimed invention" at the time the application for patent was filed.

Conclusion

8. No claims are allowed.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cynthia B. Wilder, Ph.D. whose telephone number is (571) 272-0791. The examiner works a flexible schedule and can be reached by phone and voice mail. Alternatively, a request for a return telephone call may be emailed to cynthia.wilder@uspto.gov. Since email communications may not be secure, it is suggested that information in such request be limited to name, phone number, and the best time to return the call.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (703) 308-1119. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Cynthia Wilder

CYNTHIA WILDER
PATENT EXAMINER

5/10/2004